WHAT IS CLAIMED IS:

1. A method for identifying a monomer domain that binds to a target molecule, the method comprising,

providing a library of monomer domains, wherein the monomer domains each bind an ion;

screening the library of monomer domains for affinity to a first target molecule; and

identifying at least one monomer domain that binds to at least one target molecule.

2. The method of claim 1, wherein the ion is selected from calcium or zinc.

3. The method of claim 1, wherein the monomer domain is selected from the group consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

4. The method of claim 1, further comprising linking the identified monomer domains to a second monomer domain to form a library of multimers, each multimer comprising at least two monomer domains;

screening the library of multimers for the ability to bind to the first target molecule; and

identifying a multimer that binds to the first target molecule.

5. The method of claim 1, wherein the monomer domains are between 25 and 500 amino acids.

6. The method of claim 1, wherein each monomer domain of the selected multimer binds to the same target molecule.

7. The method of claim 1, wherein the selected multimer comprises at least three monomer domains.

8. The method of claim 1, wherein the selected multimer comprises four monomer domains.

9. The method of claim 4, comprising identifying a multimer with an improved avidity for the target compared to the avidity of a monomer domain alone.

10. The method of claim 1, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

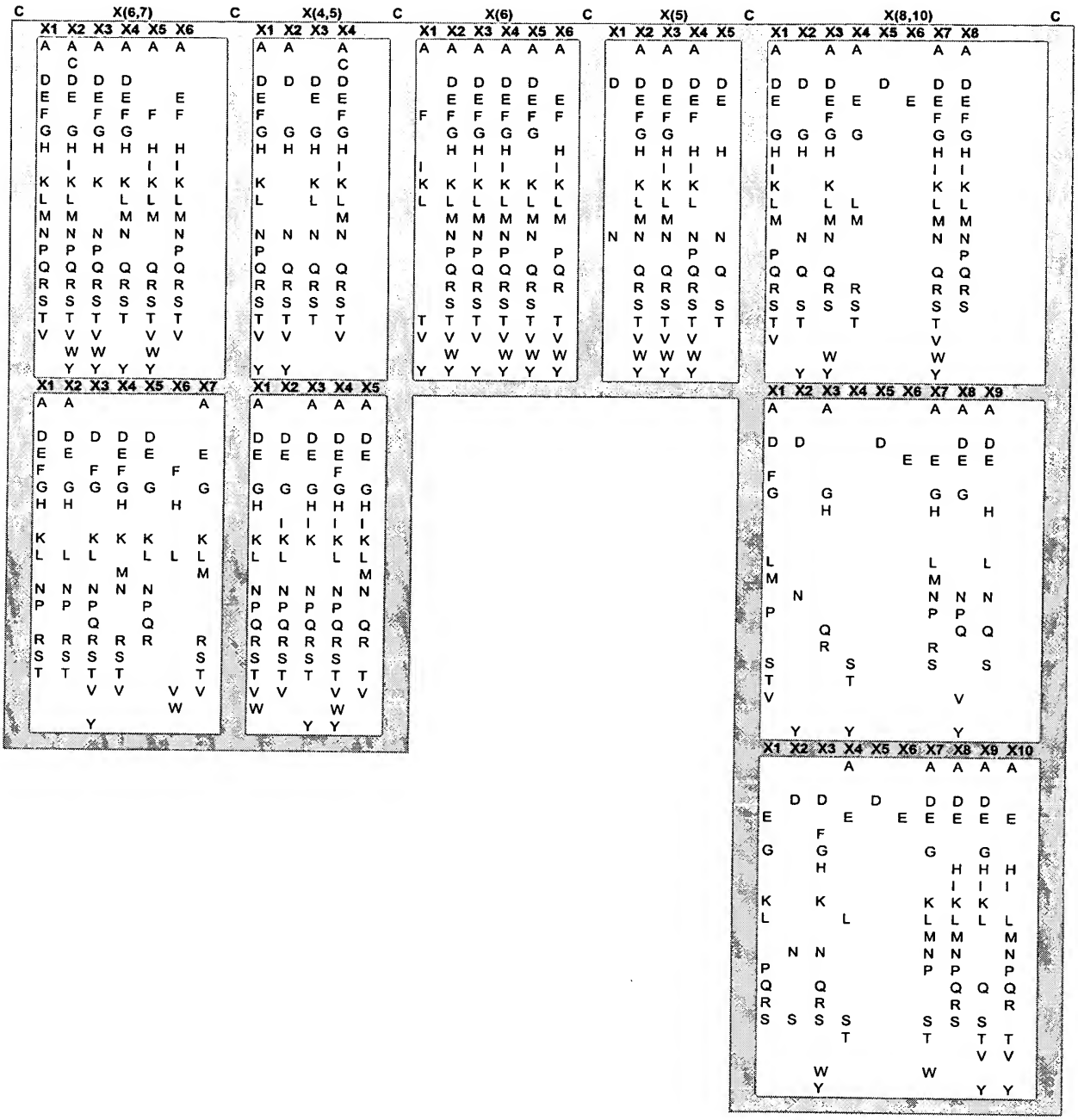
wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

11. The method of claim 10, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$CaX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$

wherein X is defined as follows:



12. The method of claim 1, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$$C_aX_{3\text{-}14}C_bX_{3\text{-}7}C_cX_{4\text{-}16}C_dX_{1\text{-}2}C_eX_{8\text{-}23}C_f$$

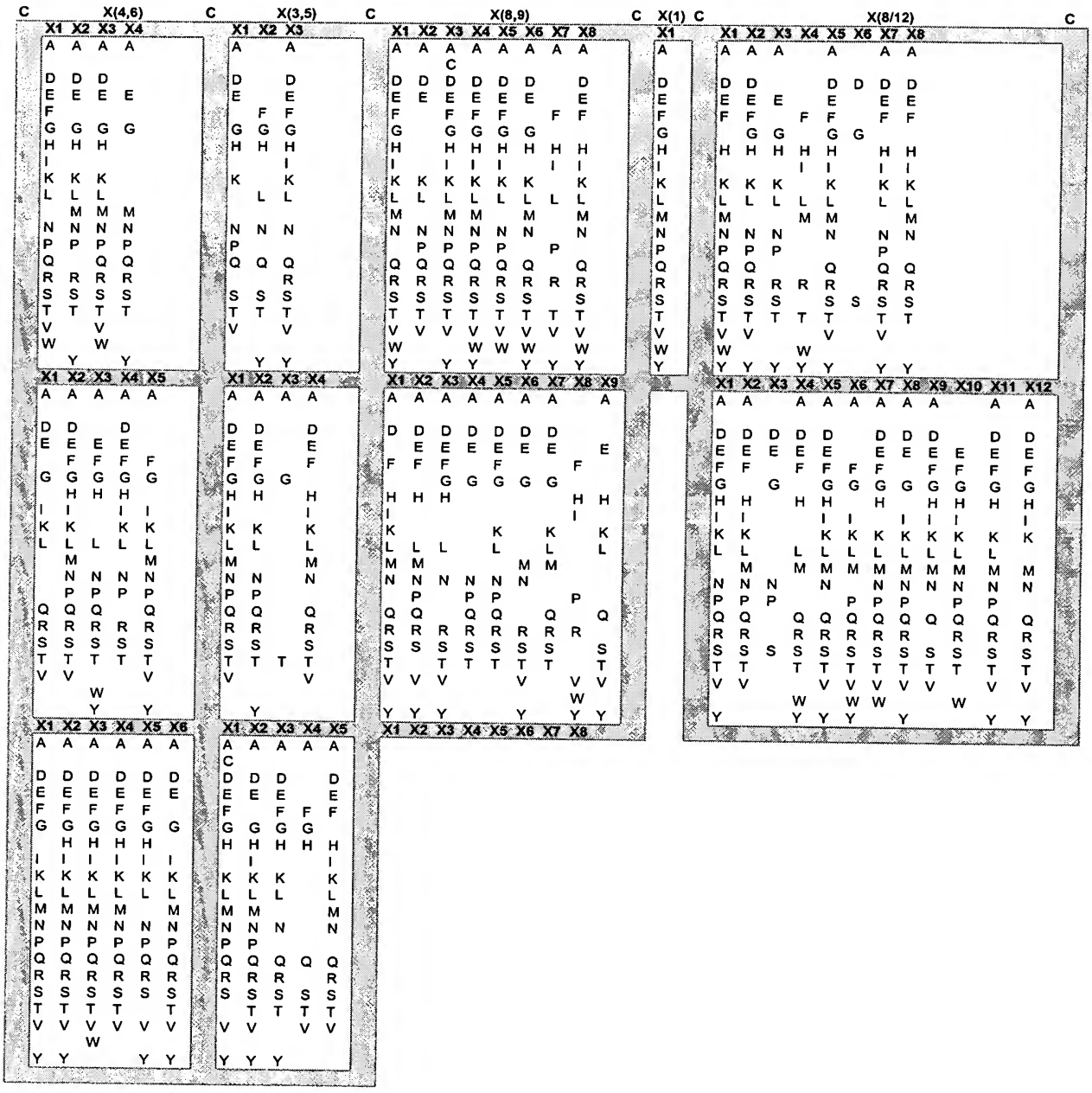
wherein C is cysteine, $X_{n\text{-}m}$ represents between n and m number of independently selected amino acids; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

13. The method of claim 10, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$$C_aX_{4\text{-}6}C_bX_{3\text{-}5}C_cX_{8\text{-}9}C_dX_1C_eX_{8\text{-}12}C_f$$

wherein X is defined as follows:



14. The method of claim 1, further comprising a step of mutating at least one monomer domain, thereby providing a library comprising mutated monomer domains.

15. The method of claim 14, wherein the mutating step comprises recombining a plurality of polynucleotide fragments of at least one polynucleotide encoding a polypeptide domain.

16. The method of claim 14, wherein the mutating step comprises directed evolution.

17. The method of claim 14, wherein the mutating step comprises site-directed mutagenesis.

18. The method of claim 1, further comprising,

screening the library of monomer domains for affinity to a second target molecule;

identifying a monomer domain that binds to a second target molecule;

linking at least one monomer domain with affinity for the first target molecule with at least one monomer domain with affinity for the second target molecule, thereby forming a multimer with affinity for the first and the second target molecule.

19. The method of claim 1, wherein the target molecule is selected from the group consisting of a viral antigen, a bacterial antigen, a fungal antigen, an enzyme, an enzyme substrate, a cell surface protein, an enzyme inhibitor, a reporter molecule, and a receptor.

20. The method of claim 1, wherein the library of monomer domains is expressed as a phage display, ribosome display or cell surface display.

21. The method of claim 1, wherein the library of monomer domains is presented on a microarray.

22. The method of claim 1, wherein the monomer domains form a secondary structure by the formation of disulfide bonds.

23. The method of claim 1, wherein the monomer domains are linked by a polypeptide linker.

24. The method of claim 23, wherein the polypeptide linker is a linker naturally-associated with the monomer domain.

25. The method of claim 23, wherein the polypeptide linker is a variant of a linker naturally-associated with the monomer domain.

26. The method of claim 23, wherein the linker is between 1-20 amino acids.

27. The method of claim 23, wherein the linker comprises the following sequence, $A_1A_2A_3A_4A_5A_6$, wherein

A1 is selected from the amino acids A, P, T, Q, E and K;

A_2 and A_3 are any amino acid except C, F, Y, W, or M;

A_4 is selected from the amino acids S, G and R;

A_5 is selected from the amino acids H, P, and R

A_6 is the amino acid, T.

28. A method of producing a polypeptide comprising the monomer domain identified in claim 1.

29. The method of claim 28, wherein the polypeptide is produced by recombinant gene expression.

30. A polypeptide comprising the monomer domain identified in claim 1.

31. A polynucleotide encoding the monomer domain identified in claim 1.

32. A method for identifying a multimer that binds to at least one target molecule, the method comprising:

providing a library of multimers, wherein each multimer comprises at least two monomer domains and each monomer domain exhibits a binding specificity for a target molecule; and

screening the library of multimers for target molecule-binding multimers.

33. The method of claim 32, further comprising identifying target molecule-binding multimers having an avidity for the target molecule that is greater than the avidity of a single monomer domain for the target molecule.

34. The method of claim 32, wherein one or more of the multimers comprises a monomer domain that specifically binds to a second target molecule.

35. A method of producing a polypeptide comprising the multimer identified in claim 32.

36. The method of claim 35, wherein the polypeptide is produced by recombinant gene expression.

37. A method for identifying a multimer that binds to a target molecule, the method comprising,

providing a library of monomer domains and/or immuno domains;

screening the library of monomer domains and/or immuno domain for affinity to a first target molecule; and

identifying at least one monomer domain and/or immuno domain that binds to at least one target molecule;

linking the identified monomer domain and/or immuno domain to a library of monomer domains and/or immuno domains to form a library of multimers, each multimer comprising at least two monomer domains, immuno domains or combinations thereof;

screening the library of multimers for the ability to bind to the first target molecule; and

identifying a multimer that binds to the first target molecule.

38. The method of claim 37, wherein the monomer domains each bind an ion.

39. The method of claim 38, wherein the ion is selected from the group consisting of calcium and zinc.

40. The method of claim 37, wherein the monomer domains are selected from the group consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

41. A library of multimers, wherein

each multimer comprises at least two monomer domains connected by a linker; and

each monomer domainbinds an ion.

42.. The library of claim 41, wherein the ion is selected from calcium and zinc.

43. The library of claim 41, wherein each monomer domain of the multimers is a non-naturally occurring monomer domain.

44. The library of claim 41, wherein the monomer domains are between 25 and 500 amino acids.

45. The library of claim 41, wherein the polypeptide domains are selected from the group consisting of consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

46. The library of claim 41, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

47. The library of claim 46, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$CaX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$

wherein X is defined as follows:

48. The library of claim 41, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$

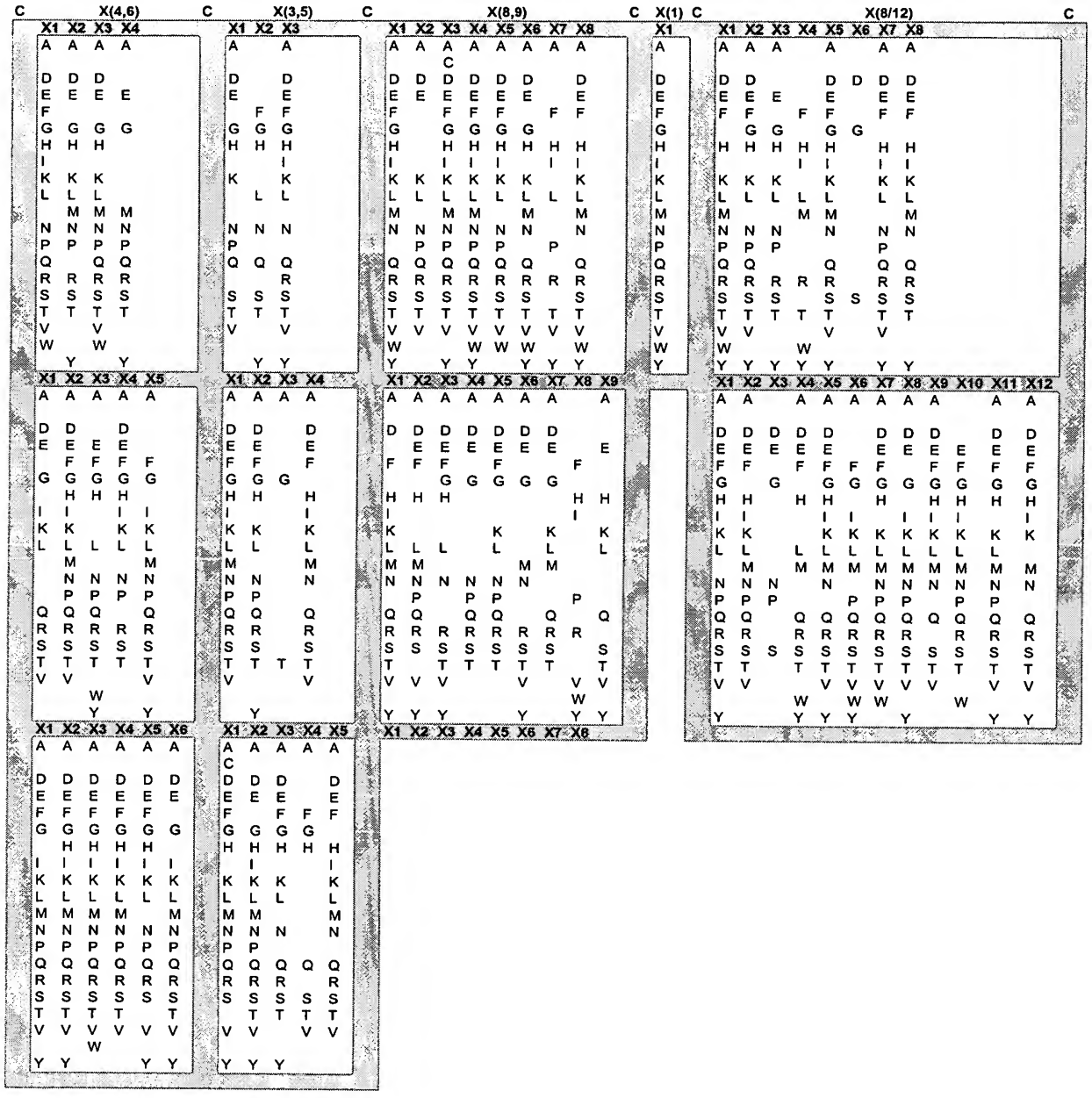
wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

49. The library of claim 48, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$$C_aX_{4\text{-}6}C_bX_{3\text{-}5}C_cX_{8\text{-}9}C_dX_1C_eX_{8\text{-}12}C_f$$

wherein X is defined as follows:



50. The library of claim 41, wherein the monomer domains are linked by a polypeptide linker.

51. The library of claim 50, wherein the linker is between 1-20 amino acid residues.

52. The library of claim 50, wherein the polypeptide linker is naturally associated with the monomer domain.

53. The library of claim 41, wherein the monomer domains form a secondary structure by the formation of disulfide bonds.

54. The library of claim 53, wherein the multimers comprise an A domain connected to a monomer domain by a polypeptide linker.

55. The library of claim 54, wherein the linker comprises the following sequence, $A_1A_2A_3A_4A_5A_6$, wherein

A1 is selected from the amino acids A, P, T, Q, E and K;

A2 and A3 are any amino acid except C, F, Y, W, or M;

A4 is selected from the amino acids S, G and R;

A5 is selected from the amino acids H, P, and R

A6 is the amino acid, T.

56. A polypeptide comprising at least two monomer domains separated by a heterologous linker, wherein each monomer domain specifically binds to a target molecule and each monomer domain binds an ion.

57. The polypeptide of claim 56, wherein the ion is selected from calcium and zinc.

58. The polypeptide of claim 56, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

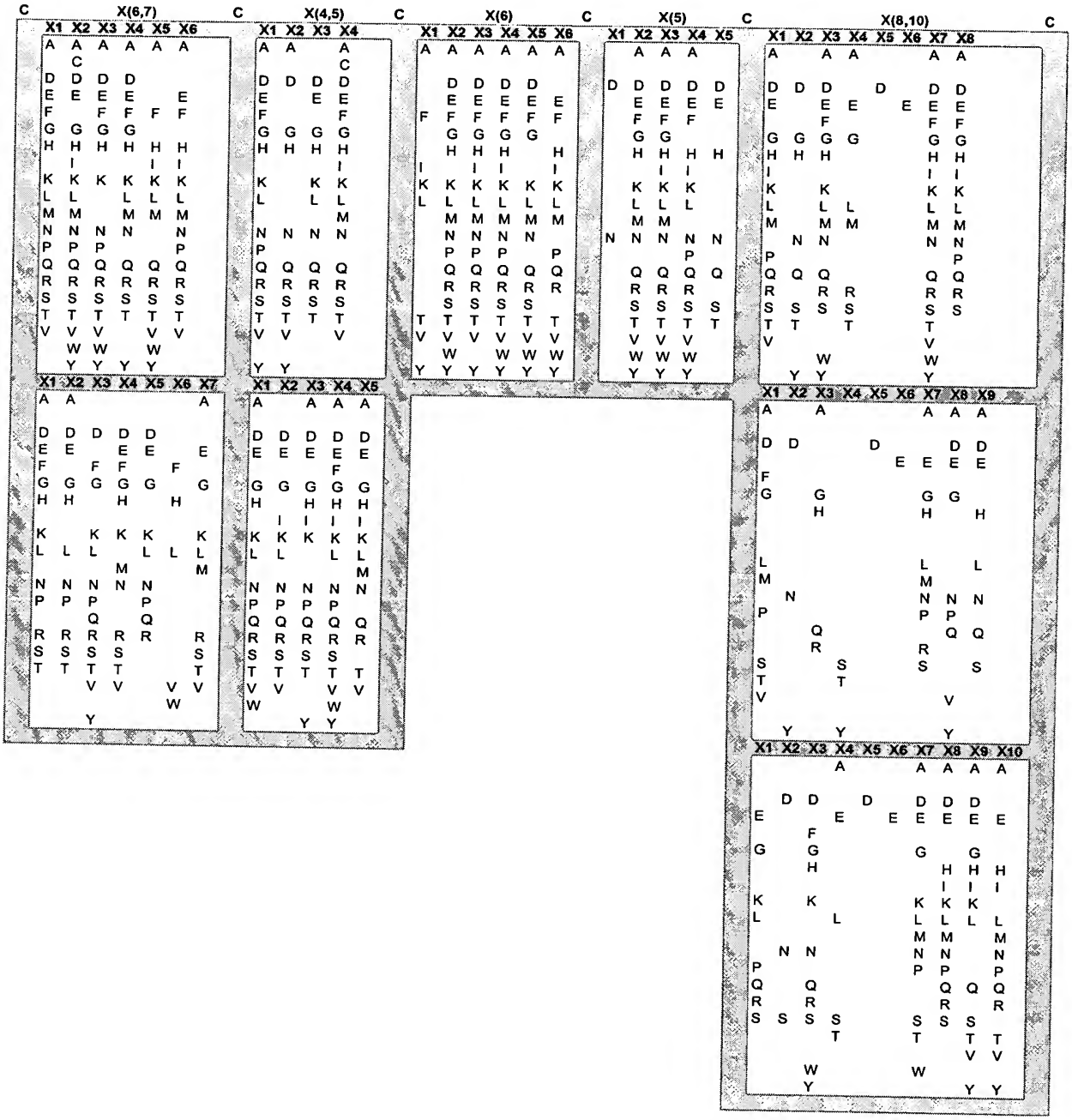
wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

59. The polypeptide of claim 58, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$CaX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$

wherein X is defined as follows:



60. The polypeptide of claim 56, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$

wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

61. The polypeptide of claim 60, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$$C_aX_{4-6}C_bX_{3-5}C_cX_{8-9}C_dX_1C_eX_{8-12}C_f$$

wherein X is defined as follows:

62. The polypeptide of claim 56, wherein each monomer domain is a non-naturally occurring protein monomer domain.

63. The polypeptide of claim 56, wherein the polypeptide comprises a first monomer domain that binds a first target molecule and a second monomer domain that binds a second target molecule.

64. The polypeptide of claim 56, wherein the polypeptide comprises two monomer domains, each monomer domain having a binding specificity for a different site on a first target molecule.

65. The polypeptide of claim 56, wherein the monomer domains are between 25 and 500 amino acids.

66. The polypeptide of claim 56, wherein the polypeptide comprises at least three monomer domains.

67. The polypeptide of claim 56, wherein the polypeptide comprises four monomer domains.

68. The polypeptide of claim 56, comprising polypeptide has an improved avidity for a target molecule compared to the avidity of a monomer domain alone.

69. The polypeptide of claim 68, wherein the avidity of the polypeptide is at least two times the avidity of a monomer domain alone.

70. The polypeptide of claim 56, wherein the monomer domain is selected from the group consisting of an A domain, EGF domain, EF Hand, Cadherin domain, C-type lectin, C2 domain, Annexin, Gla-domain, Trombospondin type 3 domain and zinc finger.

71. The polypeptide of claim 56, wherein the target molecule is selected from the group consisting of a viral antigen, a bacterial antigen, a fungal antigen, an enzyme, a cell surface protein, an enzyme inhibitor, a reporter molecule, and a receptor.

72. The polypeptide of claim 73, wherein the domains form a secondary structure by the formation of disulfide bonds.

73. The polypeptide of claim 56, wherein the monomer domains are linked by a polypeptide linker.

74. The polypeptide of claim 73, wherein the polypeptide linker is a naturally-occurring linker associated with the monomer domain.

75. The polypeptide of claim 73, wherein the linker is between 1-20 amino acids.

76. The polypeptide of claim 73, wherein the linker comprises the following sequence, $A_1A_2A_3A_4A_5A_6$, wherein

A_1 is selected from the amino acids A, P, T, Q, E and K;

A_2 and A_3 are any amino acid except C, F, Y, W, or M;

A_4 is selected from the amino acids S, G and R;

A_5 is selected from the amino acids H, P, and R

A_6 is the amino acid, T.

77. A method for identifying a human chimeric monomer domain that binds to a target molecule, said method comprising:

providing a sequence alignment of at least two naturally occurring human monomer domains from the same family of monomer domains;

identifying amino acid residues in corresponding positions in the human monomer domain sequences that differ between the human monomer domains;

generating a library of human chimeric monomer domains, wherein each human chimeric monomer domain sequence consists of amino acid residues that correspond in type and position to residues from two or more naturally occurring human monomer domains from the same family of monomer domains;

screening the library of human chimeric monomer domains for binding to a target molecule; and

identifying a human chimeric monomer domain that binds to a target molecule.

78. The method of claim 77 wherein the naturally occurring human monomer domains are LDL receptor A-domain monomers.

79. The method of claim 77 wherein the naturally occurring human monomer domains are EGF-like domain monomers.

80. The method of claim 77 wherein the screening of the library is carried out using a two-hybrid screening method.

81. A method of producing a polypeptide comprising the multimer identified in claim 77.

82. The method of claim 82, wherein the polypeptide is produced by recombinant gene expression.

83. A non-naturally-occurring polypeptide comprising an LDL receptor class A domain monomer, wherein the monomer comprises the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$

wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

84. The polypeptide of claim 83, wherein the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$CaX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$

wherein X is defined as follows:

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1 85. The polypeptide of claim 83, wherein the polypeptide is 65 or fewer
2 amino acids long.

1 86. The polypeptide of claim 83, wherein the monomer is fused to a
2 heterologous amino acid sequence.

1 87. The polypeptide of claim 83, wherein the monomer binds to a target
2 molecule.

88. The polypeptide of claim 86, wherein the heterologous amino acid sequence is selected from an affinity peptide, a heterologous LDL receptor class A domain, a heterologous EGF domain, a purification tag, an enzyme, and a reporter protein.

89. A non-naturally-occurring polypeptide comprising an EGF domain monomer, wherein the EGF domain monomer comprises the following sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$

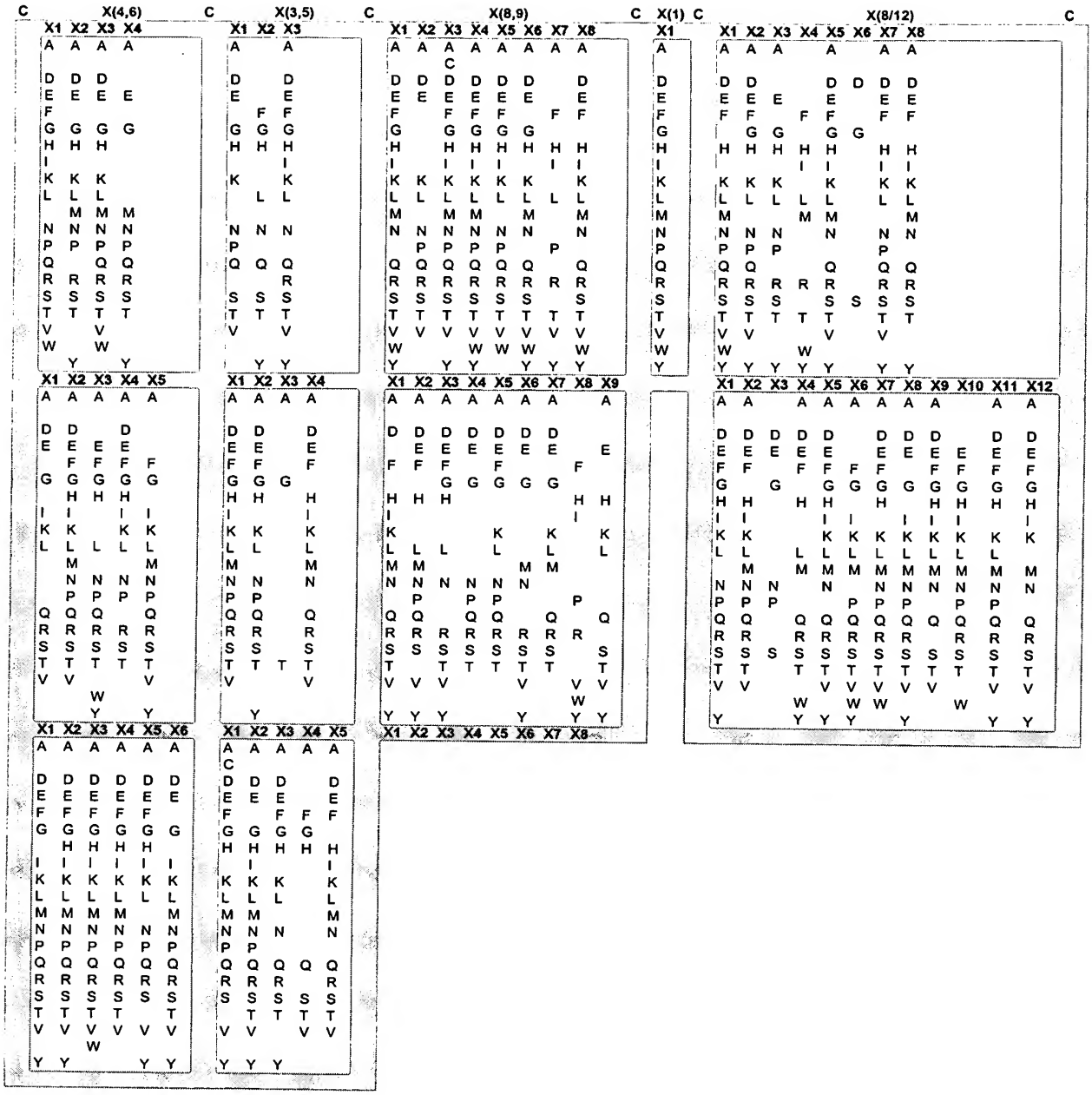
wherein C is cysteine, X_{n-m} represents between n and m number of independently selected amino acids; and

wherein C_a-C_c, C_b-C_e and C_d-C_f form disulfide bonds.

90. The polypeptide of claim 89, wherein the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{4-6}C_bX_{3-5}C_cX_{8-9}C_dX_1C_eX_{8-12}C_f$

wherein X is defined as follows:



91. The polypeptide of claim 89, wherein the EGF domain monomer is fused to a heterologous amino acid sequence.

92. The polypeptide of claim 89, wherein the monomer binds to a target molecule.

93. The polypeptide of claim 89, wherein the polypeptide is 45 or fewer amino acids long.

94. The polypeptide of claim 91, wherein the heterologous amino acid sequence is selected from an affinity peptide), a heterologous LDL receptor class A domain, a heterologous EGF domain, a purification tag, an enzyme, and a reporter protein.